Contemporary presentation and evolution of management of neck paragangliomas

Stavros K. Kakkos, MD, MSc, PhD, RVT, Daniel J. Reddy, MD, FACS, RVT, Alexander D. Shepard, MD, FACS, RVT, Judith C. Lin, MD, FACS, RVT, Timothy J. Nypaver, MD, FACS, RVT, and **Mitchell R. Weaver, MD, FACS, RVT,** *Detroit, Mich*

Background: **The aim of the present study was to review the contemporary presentation and evolution of management of neck paragangliomas.**

Methods: **Forty-one neck paragangliomas operated on in 36 patients over a 44 year period were included in the current report. The study period was divided into two parts, the first three decades (1964-1989), during which the current management techniques were evolved, and the last two decades (1990-2008).**

Results: **Patients presented with a palpable neck mass (n = 17), cranial nerve (CN) palsy (n = 3) or both (n = 6), or the lesion was an incidental finding (n = 14). The use of cross-section imaging modalities (n = 24) increased from 35% during the first part of the study to 95% during the second part of the study (*P* < .001). Preoperative embolization (introduced in 1979) was performed in 60% (median size 4.3 cm for embolized vs 3 cm [*P* = .02], for non-embolized tumors). During the first study period, the frequency of Shamblin group II/III tumors was 95% compared with a frequency of 42% during the second study period (*P* < .001, odds ratio 25), median blood loss was 600 ml and 150 ml, respectively (*P* = .001) and the transfusion rate was 44% and 5%, respectively (*P* = .008). The incidence of temporary and permanent new CN deficits postoperatively was 22.5% and 10%, respectively, and was similar during the two study periods. Three tumors were malignant, based on lymph node involvement (n = 1) or development of late metastases (n = 2).**

Conclusions: **In the modern era, neck paragangliomas can be managed with a low incidence of long-term sequelae. Smaller, asymptomatic, and incidentally detected tumors are currently the most common presentation pattern. (J Vasc Surg 2009;49:1365-73.)**

Paragangliomas, also known as chemodectomas, are rare tumors that arise from chemoreceptor cells that form the carotid and aortic bodies and the glomus jugulare, but can be also located in the ganglion nodosum of the vagus, the middle ear, and other sites throughout the body. Carotid body tumors are the most common form of neck paragangliomas (NPs). According to the operative volume statistics of the Accreditation Council for Graduate Medical Education (ACGME) for Vascular Surgery trainees, most academic centers in this country do not resect more than one tumor of this type per year,[1] although variations due to referral patterns do exist.[2-4]

Unless they are found incidentally, NPs are indolent until they grow large enough to cause symptoms like a palpable mass, cranial nerve palsy, or both. Although usually benign, resection of locally advanced tumors can be complicated by a high incidence of cranial nerve (CN) injury due to direct involvement or close proximity.[2,5-9] Involvement of the carotid artery can occasionally necessitate carotid artery reconstruction.[2,5,8] Because the mortality and neurological morbidity of tumor resection with internal carotid artery ligation was worse than the natural history of these slowly growing tumors,[10-12] expectant management was the standard treatment before the era of carotid artery reconstruction.[13] Currently, however, uncomplicated resection of these tumors is usually feasible as a result of careful preoperative planning and the use of several adjuncts, including cross-sectional imaging,[14,15] selective preoperative embolization,[16] and mandibular subluxation,[17,18] use of bipolar cautery,[19,20] selective carotid shunting based on intraoperative cerebral monitoring,[21] and carotid artery reconstruction when deemed necessary.[2,5,22]

The aim of the present study was to review the contemporary presentation and the evolution of management strategies for these complex tumors over the last five decades.

From the Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital.

Competition of interest: none.

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Reprint requests: Daniel J. Reddy, MD, Professor of Surgery, Wayne State University, John D. Dingell VA Medical Center (S-11), 4646 John R. Street, Detroit, MI 48201 (e-mail: daniel.reddy@va.gov).

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METHODS

Study design. This is a retrospective study of patients with neck paragangliomas identified from the prospectively maintained Division of Vascular Surgery,[23] and Department of Pathology databases, using the appropriate International Classification of Diseases, 9th Revision (ICD-9) and Current Procedural Terminology (CPT) codes and free-text search terms, as appropriate. Patient information was retrieved from these databases, paper charts, and hospital electronic records. To identify trends reflecting the evolution of methods and techniques used in the evaluation and management of NPs,[16] patients were divided into two groups, those treated during the early years (from 1964 to 1989 inclusive, during which the current management techniques were evolved) and the late years (between 1990 and 2008) of the study. The division of the study subjects into these two intervals was based on major changes in diagnostic modalities and techniques and the accumulation of experience in managing these rare tumors during the early study period. The Institutional Review Board of the Hospital approved the study.

Preoperative evaluation. Preoperative diagnostic testing included angiography, the only imaging method employed at the beginning of the series and cross-sectional imaging. Ultrasonography became available in the mid 1970's, followed by computerized tomography (Fig 1, online only) in the early 1980's, and magnetic resonance imaging (Fig 2, online only) in the late 1980's. Cross-sectional imaging, however, was not routinely employed until the second period of the study. Initially angiography was performed via the direct antegrade carotid puncture, but during the 1980's the retrograde femoral or brachial approach was adopted. More recently, computerized tomographic angiography has been our preferred imaging modality. Preoperative embolization to reduce intraoperative bleeding (Fig 3, online only) was introduced in 1979 and performed selectively by an Interventional Radiologist (and more recently a Neuro-Radiologist) in 21 cases thereafter, usually 24 hours before excising NPs presenting unusual technical difficulties[16] (ie, tumors that were large, belonged to Shamblin groups 2 or 3 or extended cranially). Gelfoam particles followed by spring coils delivered through a transarterial approach were used early in our series,[16] but more recently microcoils have been used exclusively (GDC-10 coil [Boston Scientific, Natick, Mass], Hydrocoil [MicroVention/Terumo, Aliso Viego, Calif], and TruFill Orbits [Cordis, Miami Lake, Fla]).

Surgical procedures. Based on tumor location as documented by preoperative imaging, excision is performed through a standard anterior sternocleidomastoid incision, as previously described by our group (Fig 4, online only),[16] or an infratemporal fossa approach for glomus jugulare tumors. Once the tumor is visualized, assessment of carotid artery involvement is performed; in such cases dissection is typically directed to achieve control of the common carotid artery, proximally and the internal and external carotid arteries, distally before attempting tumor mobilization. Distal internal carotid exposure is facilitated utilizing standard techniques (eg, ligation of the occipital artery branch to the sternocleidomastoid muscle, division of the posterior belly of the digastric muscle). Depending on tumor location, size, and degree of carotid artery involvement, a variety of operative adjuncts were adopted during the first

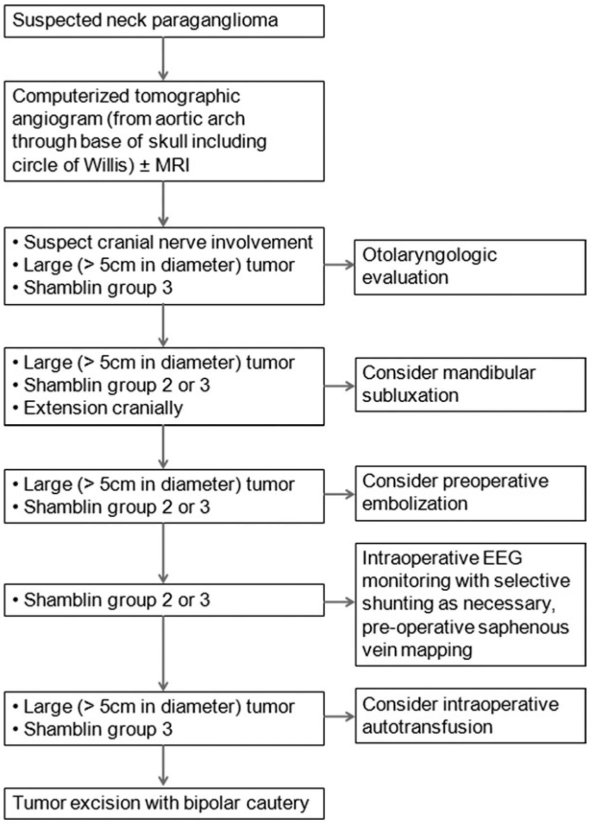

Fig 5. Flow chart of diagnostic modalities and adjunctive techniques recommended to improve safety of neck paraganglioma resection.

part of the study and thereafter used selectively (Fig 5). These adjuncts included: mandibular subluxation (introduced in 1987) for tumors extending cranially,[17,18] autotransfusion for large tumors,[12] and intraoperative cerebral monitoring with electroencephalography (EEG) (introduced in 1985) with selective shunting of the internal carotid artery as needed for carotid artery clamping and/or reconstruction.[21] To minimize CN injury, bipolar cautery is used;[20] adjacent non-involved CNs are protected and mobilized off the tumor as required; this is achieved by dissecting through the tumor pseudocapsule. To facilitate mobilization of larger tumors, external carotid artery (ECA) ligation is performed if necessary.[2] For advanced tumors encasing the internal carotid artery (Fig 6) or densely adherent to the internal and/or common carotid arteries without a dissection plane between the tumor and the vessel adventitia (white line of Gordon-Taylor), carotid artery excision is performed. Carotid artery reconstruction is usually performed with an interposition saphenous vein graft from the common carotid artery to the internal carotid. The Shamblin classification scheme is used to classify tumors in relation to carotid artery involvement.[24] According to this classification, group 1 tumors can be resected without significant trauma to the vessel wall or to the tumor

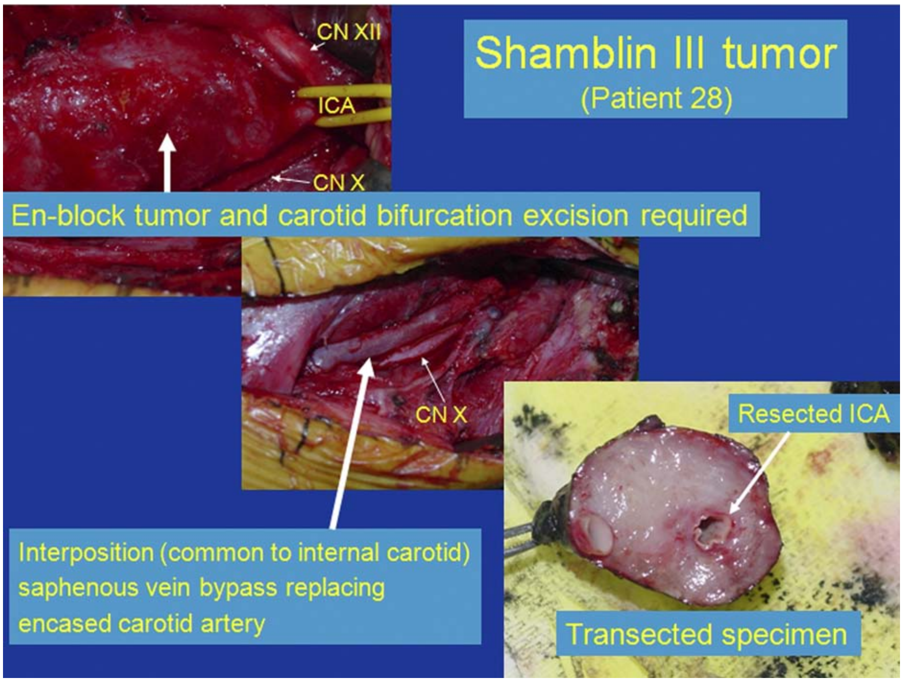

Fig 6. Excision of a Shamblin group 3 carotid body tumor that necessitated en-bloc tumor and carotid bifurcation excision followed by an interposition (common to internal carotid artery) saphenous vein bypass to replace the encased carotid artery.

capsule. Group 2 tumors partially surround the artery and are more adherent to the adventitia and, although their dissection is much more difficult, it is still possible to excise them without sacrificing the vessel. Group 3 tumors completely encase the artery and are usually best treated by sacrifice of the involved artery.

Outcome. Information on short and long-term outcome was retrieved from the above mentioned prospective databases, paper charts, and hospital electronic records and also the internet based social security death index. Permanent vocal cord paralysis due to recurrent laryngeal nerve or CN X injury was managed with injection or medialization laryngoplasty. Severe dysphagia due to CN IX or X injury was managed with percutaneous endoscopic gastrostomy (PEG), while for the purposes of airway protection in bilateral vocal cord palsy (previous contralateral palsy) a tracheostomy was considered.

Statistics. All data were entered into a Microsoft Office Access database (Microsoft Inc., Redmond, Washington, USA) and analyzed with SPSS 14.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The Kolmogorov-Smirnov test was used to test numerical data for normal distribution; normally distributed data were expressed as mean and standard deviation and compared with *t* test, otherwise they were expressed as median and interquartile range (IQR) and the Mann-Whitney test was used. Categorical data were analyzed with the chi-square (or Fisher's exact test where appropriate) and odd ratios (with 95% confidence interval; CI) were calculated to compare risk between groups. Two-tailed statistical tests were always used and a *P* value less than .05 was considered as statistically significant.

Table I. Pathology, by histologic type, in 36 patients with 41 neck paragangliomas

Histology type	*No*	*Percentage*
Carotid body tumor*	31	76
Vagal paraganglioma*	4	10
Glomus jugulare tumor	4	10
Cervical sympathetic chain paraganglioma	1	2
Undetermined origin	1	2
Total	41	100

*One patient with a vagal paraganglioma had a coexisting small carotid body tumor.

RESULTS

Patient presentation. During the study period (1964-2008), 41 neck paragangliomas were managed in 36 patients (Table I). These were carotid body tumors in 76%, but also vagal paragangliomas, glomus jugulare tumors, one cervical sympathetic chain paraganglioma, and one neck paraganglioma of undetermined organ of origin. One patient with a vagal paraganglioma had a coexisting small carotid body tumor excised during the same operative session. Patient demographics are shown in Table II. Paragangliomas located in the middle ear (n = 56), nasophar-

Table II. Patient demographics and presentation patterns by study period

	Study period			
	1964-1989 (n = 21)	*1990-2008 (n = 19)*	*P value*	*All years (n = 40)*
Age (mean ± sd, years)	49.7 ± 16.6	56.9 ± 16.0	.17	53.1 ± 16.5
Gender (male/female)	12/9	6/13	.11	18/22
Race (African American/Caucasian)	5/16	6/13	.58	11/29
Side (left/right)	7/14	11/8	.12	18/22
Presentation				
Neck mass	11 (52%)	6 (32%)		17 (42%)
Cranial nerve palsy	1 (5%)	2 (10%)		3 (8%)
Neck mass with cranial nerve palsy	5 (24%)	1 (5%)		6 (15%)
Incidental finding	4 (19%)	10 (53%)	.026	14 (35%)
Previous tumor biopsy or exploration	6 (32%)*	3 (16%)	.45	9 (21%)
Bilateral paraganglioma	3 (14%)	3 (16%)	1.00	6 (15%)
Family history of paraganglioma	1 (6%)*	2 (12%)	1.00	3 (9%)

*Data unavailable in two patients.

Table III. Preoperative evaluation and management of patients with neck paragangliomas

	Study period			
	1964-1989 (n = 21)	*1990-2008 (n = 19)*	*P value*	*All years (n = 40)*
Imaging				
Angiography	20 (95%)	13 (68%)	.04	33 (83%)
Cross-sectional imaging*	6 (35%)	18 (95%)	<.001	24 (67%)
Ultrasound	3	3		6
Computerized Tomography	3	15		18
Magnetic resonance imaging	0	10		10
Preoperative embolization (only after 1978)	12 (75%)	9 (47%)	0.096	21 (60%)

*Available in the late 1970's; 19 patients had two or three tests.

ynx (n = 2), or skull base with intracranial extension requiring concomitant craniotomy (n = 3), irrespective of carotid artery involvement, were excluded. Patient presentation is summarized in Table II. Symptomatic patients presented with a neck mass (n = 17), CN palsy (n = 3) or both (n = 6). The tumor was discovered as an incidental finding seen on imaging studies performed for other reasons in the remaining 14 patients. One of the patients in whom the tumor was an incidental finding presented with ipsilateral hemispheric transient ischemic attacks due to a 70% internal carotid artery stenosis per angiogram; histology revealed that the artery lumen was partially obliterated by focally calcified and ulcerated atherosclerotic plaque. Significantly more patients presented with a neck mass (with or without CN palsy) in time period one (n = 16) than in time period two (n = 7), compared with patients whose tumors were incidental findings (n = 4 and n = 10, respectively, $P = .015$). Sixteen CNs (VII, n = 6; VIII, n = 1; IX, n = 1; X or recurrent laryngeal, n = 4; XI, n = 1; XII, n = 2; and cervical sympathetic chain, n = 1), range 1-4, in nine patients were noted to be affected preoperatively. Palpable neck tumors with CN palsy were significantly larger (median tumor size, 5.3 cm; IQR, 4-8 cm) compared with those that had isolated CN palsy, a mass or no symptoms (3.4 cm; IQR, 2.6-5 cm, $P = .045$). Carotid body tumors were associated with fewer CN palsies compared with the remaining NPs (median number, 0 vs 1; $P = .003$).

Preoperative work-up. Preoperative diagnostic evaluation included angiography (n = 33), cross-sectional imaging (ultrasound [US], computed tomography [CT], or magnetic resonance imaging [MRI]; n = 24), or both. The use of cross-sectional imaging increased from the first to the second periods of the study from 35% to 95%, respectively ($P < .001$; Table III), with more than one modality being used in 19 patients. Preoperative embolization was performed in 60% (21 of 35) of tumors managed after 1978; ECA branches feeding the tumor were embolized in all cases, while in one patient additional blood supply from the vertebral artery was also embolized. The median size of embolized tumors was 4.3 cm vs 3 cm for non-embolized tumors ($P = .02$). In one patient, the embolization procedure was complicated by contrast-induced encephalopathy manifested as transient bilateral cortical blindness (Anton's syndrome); in another patient with bilateral carotid body tumors transient discomfort with chewing occurred after embolizing both ECAs. This masticatory "claudication" was presumed, due to an extensive decrease in the blood supply to the masseter muscle from occluding both ECAs. These symptoms slowly resolved postoperatively.

Surgical procedures. Operative details are shown in Table IV. The tumor was approached through a neck

Table IV. Operative management of neck paragangliomas

	Study period			
	1964-1989 (n = 21)	*1990-2008 (n = 19)*	*P value*	*All years (n = 40)*
Approach				
Neck incision	19 (90%)	17 (90%)		36 (90%)
Infratemporal fossa approach*	2 (10%)	2 (10%)	1.00	4 (10%)
Operative adjunctives				
Mandibular subluxation	2 (10%)	4 (21%)	.40	6 (15%)
EEG monitoring	5 (24%)	7 (37%)	.37	12 (30%)
ICA clamping**	7 (37%)[§]	3 (16%)	.14	10 (26%)
ICA shunting[#]	4 (21%)	0 (0%)	.11	4 (10%)
Operative findings				
Tumor size (median, IQR, in cm)	4.5 (3.4-6.2)	3.0 (2.3-4.5)	.016	4.0 (3.0-6.0)
Shamblin group 1/2/3**	1/11/7	11/4/4	.002	12/15/11
Operative procedures				
ECA ligation	10 (48%)	1 (5%)	.003	11 (28%)
ICA reconstruction	4 (19%)	3 (16%)	1.00	7 (18%)
ICA ligation	2 (10%)	0 (0%)	.49	2 (5%)
Blood loss (median, IQR, in ml)	600 (275-1,725)	150 (75-300)	.001	300 (138-1,000)
Transfusion (n, %)[#]	8 (44%)	1 (5%)	.008	9 (25%)
Transfused blood units (median, IQR)	0 (0-4)	0 (0-0)	.004	0 (0-0.5)
Transfused blood units (total)	34	1		35

IQR, Interquartile range.
*For glomus jugulare paragangliomas.
**Not applicable in 2 patients.
[#]Unknown in 2 patients.
[§]Routine shunting in all four patients in the absence of intraoperative monitoring.

Table V. Postoperative cranial nerve injury

	Study period			
	1964-1989 (n = 21)	*1990-2008 (n = 19)*	*P value*	*All tumors (n = 40)*
Permanent CN injury, no of patients (%)	3 (14.3%)	1 (5.3%)	.61	4 (10%)
Temporary CN injury, no of patients (%)	4 (19%)	5 (26%)	.71	9 (22.5%)
All CN injuries, no of patients (%)	7 (33%)	6 (32%)	.91	13 (32.5%)
All CN injuries, sum (median no) of affected nerves	14 (0)	8 (0)	.61	22 (0)

CN, Cranial nerve.

incision (n = 36) or an infratemporal fossa approach (n = 4). During the first study period, one patient with a history of vocal cord palsy due to prior excision of a contralateral carotid body tumor involving CN X underwent a prophylactic tracheostomy. A difference in utilization rates for operative adjuncts was observed between the two study periods, with mandibular subluxation and EEG monitoring been more frequent during the second period; a reverse trend in ICA clamping and shunting rates was also seen. Tumors during the first period of this study were significantly larger and more advanced than in the second period. During the first study interval, the frequency of Shamblin group 2/3 tumors was 95% and during the second 42% ($P < .001$; odds ratio, 25). External carotid ligation was utilized almost exclusively during the first period of this study, when it was performed in half of all patients. Carotid reconstruction (bypass with a Dacron graft, n = 1 or saphenous vein graft, n = 4, ICA patch angioplasty using an ECA flap, n = 1, and ECA-ICA transposition, n = 1) or ICA ligation (n = 2, because of history of previous radiation in one case) was necessary in 82% of Shamblin group 3 tumors. The difference in median blood loss between the first and second intervals of the study, 600 ml and 150 ml, respectively, was significant ($P = .001$) as was the transfusion rate, 44% and 5%, respectively ($P = .008$). Complete tumor resection was accomplished in 38 patients (95%). In one patient, residual tumor involving CNs IX-XII was left behind. In another elderly patient with a number of comorbidities treated during the 1960's, a preoperative plan to excise a tumor encasing the ICA was abandoned during neck exploration with lymph node biopsy only.

Postoperative complications. Twenty-two CNs in 13 patients demonstrated evidence of dysfunction, postoperatively (Table V); these were CN VII branches (n = 4, including the marginal mandibular branch, n = 3 and the marginal mandibular, buccal, and temporal branches, n = 1), CN IX (n = 3), CN X (n = 5), recurrent laryngeal nerve (n = 2), CN XI (n = 2), CN XII (n = 3), and sympathetic chain (n = 3). Two cases of CN X palsy were observed in patients operated on for vagus paraganglioma. An additional patient with a vagal paraganglioma, causing dysphagia and hoarseness preoperatively, had worsening of these symptoms postoperatively requiring placement of a gastrostomy tube. Three more patients without preoperative dysphagia (all with carotid body tumors) required temporary feeding tube placement because of CN IX (n = 2) or CN X (n = 1) injury. Persistent vocal cord paralysis due to permanent (preoperative or postoperative) CN X or recurrent laryngeal nerve palsy was managed with injection laryngoplasty in five patients with good results, except one of them who required an additional medialization laryngoplasty with a Silastic implant. New permanent CN deficits were seen postoperatively in 10% of all patients, while new temporary CN deficits were seen in 22.5%. There was no association between baseline patient and tumor characteristics (including size, location, group, and symptoms or study period) and new postoperative CN injury; this occurred in 33% of carotid body tumors and 30% of the remaining tumor types ($P = 1.00$), while its incidence in Shamblin group 1, 2 and 3 tumors was 25%, 40%, and 36%, respectively. There was an association between adjunctive treatment modalities and new postoperative CN injury, with NPs that required mandibular subluxation or ICA clamping being associated with an increased incidence of CN injury (67% and 50%, respectively) compared with those that did not require these maneuvers (27% ($P = .075$) and 25% ($P = .24$), respectively]. The median size of tumors in patients who developed permanent postoperative CN injuries was larger (8 cm) than in patients who sustained no such injuries (3.8 cm), ($P = .08$) and tumors developing permanent postoperative CN injury were more frequently malignant (50%) and larger (5.9 cm) compared with those removed with no neurological sequelae (2.8% malignant, $P = .022$ and 4 cm, $P = .19$, respectively). Additional complications included neck wound hematoma requiring re-operation in two patients, thigh wound hematoma (following saphenous vein harvesting, n = 1, managed conservatively), and stroke, one fatal in a patient who had ICA ligation, a second one in a patient requiring carotid bypass who made a partial recovery (both during the first decade of the study), and a third stroke that occurred two weeks postoperatively in a patient requiring carotid bypass; this was patent and the patient made a full recovery (during the second part of the study). There were no other deaths.

Long-term follow-up. Three tumors (7.5%, two carotid body tumors and one vagal paraganglioma) were malignant, based on lymph node involvement (confirmed histologically, n = 1) or development of late metastases (n = 2). The first of the two patients who developed late metastases, developed these six years postoperatively at the L2 vertebra; local tumor recurrence was also evident. The vertebral body metastases were initially managed with radiotherapy and later with L2 vertebrectomy and anterior spinal fixation with sequential embolization. The local recurrence was managed expectantly with the patient living five more years. The second patient developed pulmonary metastases four years after resection of a vagal paraganglioma. These have been managed expectantly and the patient is still alive after two years of follow-up. Two additional patients developed local recurrence. One patient, 17 years after complete excision of a carotid body tumor, developed local recurrence that was re-excised. This second procedure was complicated by permanent vocal cord paresis and temporary dysphagia due to apparent CN X injury and a temporary CN XII injury. He is recurrence-free three years later. The second patient, four years after complete excision of a glomus jugulare tumor, developed a local intracranial recurrence. Finally, the patient with known residual disease after excision of a vagal paraganglioma and a small carotid body tumor (treated with radiosurgery) developed late tumor progression with palsy of CNs IX-XII. Ten and twenty year patient survival was 81% and 63%, respectively.

DISCUSSION

In this study, we reviewed the presentation and management patterns of NPs treated over a period of five decades. Significantly smaller and less advanced NPs with more precise preoperative imaging were seen in the most recent period, and were associated with a significant reduction in operative blood loss and transfusion rates. At the beginning of the series, preoperative diagnostic testing included only angiography initially via the direct antegrade carotid puncture. After a decade, cross-sectional imaging became available, initially in the form of ultrasonography in the mid 1970's, followed by computerized tomography in the early 1980's and magnetic resonance imaging in the late 1980's. Adjuncts to facilitate resection and prevent complications were also introduced, including preoperative embolization in 1979, intraoperative cerebral monitoring with EEG and selective shunting of the internal carotid artery in 1985, and mandibular subluxation in 1987.

Over the course of the entire study, the frequency of NPs detected incidentally rose from 19% to 53%. The widespread utilization of non-invasive imaging methods explains the increased frequency of asymptomatic (and smaller) tumors observed during the second part of our study and could also be responsible for the older age of this group. More importantly, cross-sectional imaging modalities (CT scanning and MR imaging) have significantly improved preoperative planning. The goals for preoperative imaging, as summarized by Iafrati and O'Donnell, are to secure the diagnosis (biopsy being contraindicated because of the highly vascular nature of these tumors), to define local tumor extension to anticipate the need for extended exposure or carotid resection, to evaluate the presence of concomitant atherosclerotic carotid disease, potentially requiring endarterectomy, to identify synchronous tumors either ipsilateral or in the contralateral carotid, and finally to determine of the need for preoperative tumor embolization.[25] A correct preoperative diagnosis is important to minimize unnecessary neck exploration and/or biopsies;[20,26,27] reflecting the utility of preoperative imaging, the rate of unnecessary tumor exploration and/or biopsies in our series fell from 32% in the early period to 16% in the later period, consistent with the experience of others.[28] Utilization of cross-sectional imaging (CT scanning or MR imaging) was almost universal during the second part of our study. Similarly, in a recent multicenter study multiple cross-sectional imaging modalities, including ultrasound were frequently used.[7] In contrast, ultrasound was rarely used alone in our series, because it cannot provide details on tumor extension. Angiography was used less often during the second part of our series, which indicates a trend for selective usage, consistent with previous reports,[7] mainly for the purposes of preoperative embolization,[25,29] and rarely to assess for ICA invasion,[29] or to perform an ICA balloon occlusion test on the rare occasion ICA ligation is considered instead of reconstruction. However, some authorities continue to use angiography routinely.[28] In the modern era, high-resolution CT angiography is probably the best initial test because it combines the advantages of both axial CT scanning and angiography. Magnetic resonance imaging should be reserved for cases where precise delineation of tumor extent is required, because of its better soft tissue definition.[30]

Preoperative embolization was used in 60% in our series. Variable rates, up to 40%-50%, have been reported by others.[4,14,31,32] Consistent with our previous experience,[16] and the literature,[14,32] embolized tumors in the current study were bigger than non-embolized tumors. Reduced blood loss in embolized mid-sized tumors has been reported;[6] however, there is debate as to whether the benefits of embolization outweigh its risks,[32] mainly TIA and stroke,[33,34] as well as its additional costs. We currently recommend that preoperative embolization be considered only for NPs presenting unusual technical difficulties – tumors that are large (>5cm in size), belong to Shamblin group 3, or extend significantly cranially.

Operative challenges and hazards, recognized for over a century, can be anticipated from preoperative imaging studies and managed accordingly.[2,24] Mandibular subluxation, reserved for large tumors that usually extend cranially,[18] was performed in 15% of our cases; this method displaces the vertical ramus of the mandible forward by 2 to 3 cm transforming the normal triangular shaped operative field into a rectangular one, widening its apex, thus providing additional space for safe exposure and control of the distal ICA.[18] The Shamblin classification scheme reliably predicts the need for ICA reconstruction or ligation. Carotid reconstruction to resect an advanced tumor that encases the ICA was performed in 18% of our patients. Similar rates of carotid reconstruction, in the range of 6% to 33%, have been reported by others.[2,4,5,8,20,26,33,35,36] Carotid reconstruction is also required more often with larger tumors.[22]

Postoperative stroke was observed in 7.5% of our patients; this is associated with carotid reconstruction or ICA injury and thrombosis, and has been reported to occur in 0% to 16% of patients.[2,9,20,26,32,36] There are a variety of mechanisms for stroke in patients undergoing NP resection. Carotid clamping or ligation (as in one of our patients) can lead to brain ischemia or embolism especially in case of inadequate anticoagulation. Thrombosis of a carotid reconstruction (graft or other type), either early or delayed is usually due to technical reasons, but can result from venous graft endothelial injury or inadequate use or resistance to conventional antiplatelets, etc. In order to minimize stroke occurrence in patients requiring carotid reconstruction, we recommend monitored anticoagulation, neuromonitoring, and selective shunting intraoperatively, and antiplatelet use with ultrasound surveillance of the reconstruction postoperatively. Two cases of postoperative stroke complicated carotid reconstruction in our series. The first one was observed in a patient who had an interposition Dacron graft placed in the 60's (exact stroke mechanism unknown) while the second one (manifested on postoperative day 14) was observed in a patient with a patent venous interposition graft. To prevent stroke related to temporary carotid clamping, selective internal carotid shunting has been used in most series.[36,37] This is currently our preferred method; we routinely use EEG monitoring when resecting Shamblin group 2 or 3 tumors or in other high-risk situations where carotid clamping and/or reconstruction seems likely.

Obviously, tumors that extend up to the skull base represent a special challenge that require the assistance of surgeons experienced with the appropriate exposure(s).[38] Once frequently performed, ligation of the external carotid artery to facilitate tumor mobilization is rarely performed today. The smaller size of tumors being treated in the modern era and the availability of preoperative embolization has made this maneuver largely unnecessary.

Blood loss and transfusion rates were significantly reduced in the second part of our series. Consistent with our study, blood loss in the modern era is generally low,[14,34,39] but can average as much as 2,200 ml in Shamblin group 3 tumors.[8] Transfusion rates as high as 50% were reported in older series,[9] when cross-matching for 4-6 units of blood was frequently advised.[10,20] Compared with a standard dissection technique where the tumor is stripped away from the bifurcation in a caudocranial fashion, a craniocaudal direction of dissection has been shown to be associated with reduced blood loss,[39] very similar with the amount we reported during the second part of our study. Proponents of this approach feel that it may be superior because it allows for control of feeding branches of the external carotid before dissecting the tumor proper.

The incidence of postoperative CN dysfunction in our study was 32.5% and remained constant throughout the study period, a finding consistent with other reports in the literature.[2] Cranial nerve injury is not uncommon in carotid surgery, including both endarterectomy[40-42] and carotid body tumor excision.[2,6,7,14,20,26,32,33,35,36] Most series of carotid body tumors report a 40% incidence of CN injury,[2,6,26,32,36] but rates lower than 20%[7,35] or as high as 50%[14,33] have been documented. Permanent CN injury occurs in 8%-39% of patients,[5,6,9,14,26,33] on average 20%.[5,6,26] In our study, such injury rates were in the lower range, although we considered preoperative CN palsies, even if they were permanent, separately. Cranial nerve injury has been reported more often with advanced tumors,[43] carotid reconstruction,[4] and also glomus jugulare or vagal paragangliomas.[44] In our series, mandibular subluxation and ICA clamping were associated with an increased incidence of CN injury compared with those that did not require these maneuvers. Both of these maneuvers are associated with more difficult tumor resections. The region around the distal ICA has been described by Hallett and colleagues as the most dangerous dissection zone because of its proximity to a number of CNs which must be protected.[2] Prompt recognition and management of CN IX or X injury is imperative because the resulting aspiration can be fatal,[42] and more common in case of delayed or no use of PEG.[44,45] Prophylactic tracheostomy, once a common practice,[45,46] is currently performed selectively, only if airway complications arise.[9]

Resection of NP has a mortality rate of 1%-2%,[7,47] which, in a recent large study, was increased to 8.8% in patients requiring concomitant carotid reconstruction.[47] These data justify early tumor extirpation, which is additionally justified because of the potential for malignancy. The malignancy rate was 7% in our series and has reported to vary between 4%-14% in the literature[4,5,7,9,11,26,34,35] Because of the high complication rate of surgery that is performed for a slowly growing tumor (on average 4 mm per annum),[10] with a low malignant potential, there is debate on the need to resect all NPs.[48,49] Counterarguments include the fact that complete resection is almost always possible,[49] recurrence is rare, with reported rates varying between 4%-15%,[20,31] and most important, resection can prevent tumor-related CN palsies. Because the latter usually develop late, conservative management has been proposed in selected patients with a short life expectancy.

Management of NPs did involve a variety of specialists in our series. A multidisciplinary approach is recommended,[20,22,34,50] which may explain the better outcomes achieved in academic centers.[47] Such an approach does require a number of specialists, including radiologists to provide detailed preoperative imaging and perform preoperative tumor embolization when necessary. Otolaryngologic surgeons are helpful to evaluate patients for cranial nerve dysfunction preoperatively and to manage postoperative vocal cord problems due to recurrent laryngeal nerve or CN X injury. The infratemporal approach for glomus jugulare tumors is also performed by otolaryngologic surgeons. Mandibular subluxation is performed by a maxillofacial surgeon. Postoperative swallowing difficulties may call for a percutaneous gastrostomy tube, which can be placed by an endoscopist or radiologist. All these specialists assist the vascular surgeon to safely excise the tumor and manage postoperative complications.

In conclusion, NPs can be managed with a low incidence of long-term sequelae. Diagnosis of smaller and asymptomatic tumors is increasingly common. Improved outcomes have resulted from more complete preoperative imaging and the routine use of several operative adjuncts, including pre-operative embolization, mandibular subluxation, and intraoperative EEG monitoring.

AUTHOR CONTRIBUTIONS

Conception and design: SK, DR
Analysis and interpretation: SK, DR
Data collection: SK, JL, TN, MW
Writing the article: SK, DR, AS, JL, TN, MW
Critical revision of the article: AS
Final approval of the article: SK, DR, AS, JL, TN, MW
Statistical analysis: SK
Obtained funding: N/A
Overall responsibility: SK, DR

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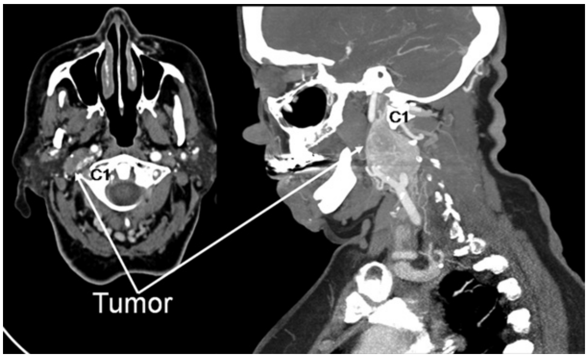

Fig 1, online only. Computerized tomographic scan with axial slices (left side) and sagittal reconstructions (right side) of a large right-side carotid body tumor extending to the level of the C1 vertebra.

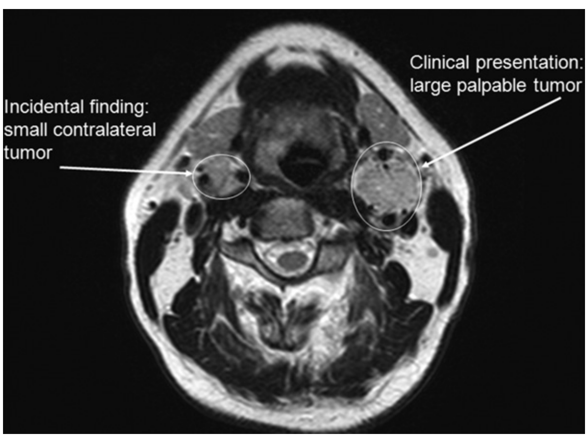

Fig 2, online only. Magnetic resonance imaging scan of a patient with bilateral carotid body tumors.

Fig 3, online only. **a**. Diagnostic preoperative right carotid artery angiogram of the patient with the carotid body tumor shown in Fig 1, which demonstrates a hypervascular tumor, splaying the carotid bifurcation. **b.** Appearance following tumor embolization/coiling with significantly reduced vascularity.

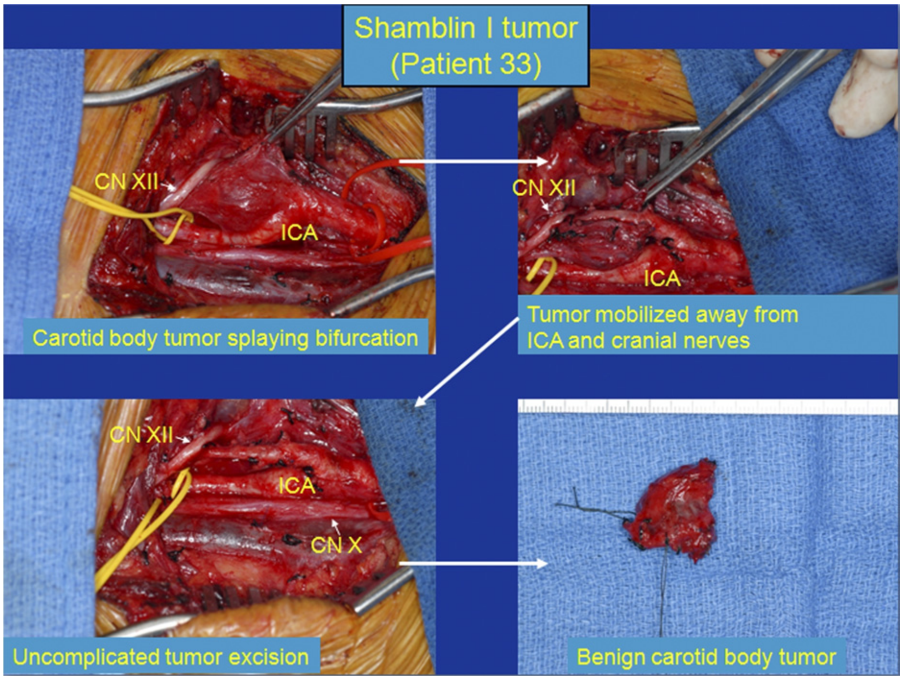

Fig 4, online only. Excision of a Shamblin group 1 carotid body tumor.